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Patients beliefs on intravenous and subcutaneous routes of administration of biologics for severe asthma treatment: A cross-sectional observational survey study

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ABSTRACT

Background: Understanding how patients generate preferences for administration route alternatives may improve health-care delivery and clinical outcomes. Recently, novel biological therapies with subcutaneous (SC) and intravenous (IV) administration routes have been approved for severe uncontrolled asthma. The aim of our study was to assess the preferred route of biologic therapy administration and related beliefs among patients with severe uncontrolled asthma.

Methods: We conducted a cross-sectional observational survey study. Patients answered an anonymous, self-administered questionnaire after an outpatient visit in pulmonary disease clinics located throughout Italy. Socio-demographic and clinical information together with the 12-Item Short Form Survey (SF-12), Work Productivity Impairment Scale and the medical resources utilization module of the Health & Work Survey were collected. Patients beliefs and preference towards SC and IV administration were investigated by means of an *ad hoc* 13 item questionnaire.

Results: the main findings: 150 patients fulfilled the inclusion criteria and completed the questionnaire (47.3% males). Preference for IV and SC administration was 18.7% and 81.3%, respectively. Compared with patients preferring SC formulation, patients that favored IV were older ($p = 0.04$), less likely to escalate corticosteroid dose ($p = 0.03$) and had emergency room (ER) access ($p = 0.009$) during asthma exacerbations. Patients felt that SC was more convenient than IV, but this belief was not associated with higher likelihood of preferring SC administration. IV formulations were more likely associated with quicker and more effective drug action ($p = 0.0001$), procedural safety and medical oversight ($p = 0.0002$) and social support ($p = 0.007$). Predictors of IV preference were represented by the association of worse asthma control and increased use of ER services, and by beliefs toward formulation effectiveness/efficiency in reducing symptoms ($p = 0.04$ and $p < 0.0001$, respectively). The model achieved excellent discrimination of administration route preference (area under the curve = 0.87).

Conclusions: Preference is guided by partially misleading beliefs, which may generate wrong expectations that in turn can affect treatment satisfaction and adherence. Convenience and efficacy beliefs for drugs with different routes of administration always should be discussed with patients to achieve informed shared-decision making.

Trial registration: Not applicable.

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Background

Patient involvement in Shared Decision Making (SDM) is gaining increasing emphasis in health care policies.[1,2] Within the collaborative process with their health care professionals, patients are provided with detailed information about treatment and medical options, and their preferences are discussed in a supportive communication in order to obtain a shared decision.[3] Besides preferences, patients' beliefs and attitudes towards medication should also be elicited as they may be associated with treatment adherence.[4–6] Hence, shared decision making should be particularly encouraged for long-term management of chronic conditions[7] as it has been shown to have a relevant role in fostering medication adherence.[8]

Patients' preferences acquire greater importance when treatment choices are equally effective and management options may be valued, yet help patients develop more accurate expectations of treatment outcomes.[9]

Particularly, patients' preference for injection routes of administration (i.e. intravenous, subcutaneous, intramuscular) achieves a prominent role as it accounts for different potential advantages or drawbacks considering dose, frequencies and duration of administration, associated pain or discomfort, treatment speed of action, safety profile, and home or hospital setting for drug delivery.[10]

Once equal safety and efficacy parameters have been established, considering patients' preferences for route of administration should be an essential principle for clinicians to consider in order to better ensure patient compliance.[10]

Head-to-head studies comparing intravenous (IV) and subcutaneous (SC) routes of administration suggest the latter being the preferred method of drug administration by patients because it is associated with home setting treatment, saved time, overall reduced discomfort and fewer complications related to poor vein access.[11] However, these studies focused on specific drugs whose available routes of administration may substantially vary, since SC formulation allows the possibility of home-based self-injection (e.g. anti-TNF agents, immunoglobulin, insulin) as well as a significant reduction of infusion duration (e.g. trastuzumab, rituximab). Conversely, IV route may be preferred, as hospital care setting appears to be associated with a safer treatment and the reassuring effect of physician presence.[12,13]

Among biologic therapies traditionally delivered by IV formulation, SC route of administration has increasingly been licensed, thus offering to patients a comparable alternative.[14] So far, patient preference studies comparing IV and SC for biologic therapies have mainly focused on inflammatory bowel disease,[15–17] breast cancer,[18] rheumatoid and psoriatic arthritis.[12,13,19]

For the treatment of severe uncontrolled asthma, different monoclonal antibodies (mAbs) have proven effective.[20] Recently, mABs directed against interleukin (IL)-5 (mepolizumab and reslizumab) and its receptor showed efficacy for patients with uncontrolled severe asthma in whom eosinophils play a dominant pathobiologic role,[21] and they have been approved as add-on therapies by the U.S. Food and Drug Administration and the European Medicines Agency. These drugs are available for IV or SC formulation and may vary in reference to dosage and frequency of administration.[22,23] Although in a 10-patient study, weight-adjusted IV reslizumab showed better clinical outcomes as compared to fixed-dose SC mepolizumab,[24] head-to-head studies comparing IV or SC administration for different mAbs are limited and superiority is difficult to determine.[17,25] Additionally, no studies so far have investigated preferences for IL-5 mABs IV or SC formulation among patients with uncontrolled severe asthma. Understanding how patients generate preferences for administration route alternatives may improve health-care delivery and clinical outcomes, thus providing physicians with better knowledge when approaching SDM.

The aim of our study was to assess the preferred route of biologic therapy administration and related beliefs among patients with severe uncontrolled asthma.

Methods

Design and setting

We conducted a cross-sectional observational survey study. Patients answered an anonymous, self-administered questionnaire after an outpatient visit in pulmonary disease clinics located throughout Italy. We enrolled adult patients younger than 75 years of age, without chronic respiratory tract comorbidities (i.e. chronic obstructive pulmonary disease, pulmonary fibrosis, emphysema, and cancer), and we restricted study inclusion to patients with poorly controlled asthma as determined by Asthma Control Questionnaire 6-item score (ACQ-6) ≥ 1.5[26–28] despite use of medium/high dose of inhaled corticosteroids/beta-adrenergic agonists combinations in the previous 12 months. Patients receiving a biologic therapy for severe asthma were not excluded from the study. No personal identifiers can be deducted from the answers to the questionnaire. After filling in the questionnaire, patients put the survey packet into an anonymous envelope and returned it to a study assistant so that patients' answers could not be matched to subjects' identity. According to the Italian regulation,[29] cross-sectional survey research based on anonymous questionnaires do not require ethical committee approval.

Measures

The questionnaire packet included a brief screener questionnaire (BSQ) tapping socio-demographic (i.e. age, geographic region, gender) and clinical information (diagnosis of asthma, presence of any other lung diseases, assessment of asthma control, concurrent asthma related treatments and routes of administration, remedies to exacerbations occurred in the previous 12 months). Responses to the BSQ were used to determine study eligibility. Furthermore, we collected information concerning patients' history of exacerbations according to expert consensus definition[30]; in order to facilitate patients' recall of exacerbation episodes occurred in the previous 12 months we provided the event definition as a primer: "*Exacerbations - commonly referred to as asthma attacks or acute asthma - are episodes of progressive increase in shortness of breath, cough, wheezing, chest tightness, or a combination of these symptoms which occur despite the regular assumption of usual therapy. When an exacerbation occurs, it is required to assume a systemic corticosteroid treatment or at least a doubling of existing dose for maintenance oral corticosteroid and/or a hospitalization and/or an emergency department visit*". We asked to report the frequency of episodes occurred in the past 12 months and recourse to hospitalization, emergency room visits, corticosteroid therapy initiation or dose escalation. We also collected employment status according to the International Labour Office definition and past/current exposure to potential occupational or environmental risk factors for asthma.

Additionally, the questionnaire packet included the 12-Item Short Form Survey (SF-12), Work Productivity Impairment Scale, and the medical resources utilization module of the Health & Work Survey[31–33] (Additional file 1).

Patients beliefs on IV and SC route of administration of biologic therapy

Since no valid scale tapping patients' beliefs toward IV/SC administration route exists, we were forced to devise an *ad hoc* scale for the study. Seventeen items (i.e. beliefs) were generated by literature review and expert opinion (Additional file 2).[10,13,34] Before answering the beliefs scale, patients were primed with statements describing the indication for biologic therapy and the procedure involved for both IV and SC administration modality (Additional file 3). Patients were asked to rate how much they believed that either one of the two administration modalities was characterized by the 17 attributes generated, which were pertaining to four factors: a) procedural safety and medical oversight (e.g. "*It allows a closer medical oversight during drug administration*"); b) efficacy and speed of action (e.g. "*It allows greater speed of action of the drug (the drug takes effect earlier*"); c) social support (e.g. "*It allows to have closer*

Table 1
Factor analysis and related reliability concerning beliefs towards IV and SC route of administration.

Beliefs (items)	Convenience	Social support	Procedural safety	Efficacy
Allows greater safety during administration	0.184	0.521	0.549	−0.078
Allows a closer medical oversight during drug administration	0.101	0.134	0.864	0.199
Allows to receive treatment in a protected and safe setting	0.039	0.123	0.870	0.172
Allows greater drug efficacy	0.118	0.492	0.333	0.521
Allows greater speed of action of the drug (the drug takes effect earlier)	−0.005	0.264	0.265	0.742
Allows less frequent drug administration	−0.031	−0.046	0.025	0.828
Allows greater convenience	0.736	0.038	−0.025	0.238
Allows less time spent managing asthma	0.755	0.127	−0.036	0.018
Allows to have more time for non disease-related daily activities	0.779	−0.144	0.119	−0.205
Allows to have less hassles about asthma	0.703	0.172	0.344	−0.069
Allows a better interactions with the medical staff	0.023	0.775	0.004	0.322
Allows to interact with other patients and share worries and concerns	0.302	0.664	0.100	−0.041
Allows to have closer relationships with medical staff	−0.211	0.797	0.263	0.070
Cronbach Coefficient Alpha	0.751	0.689	0.781	0.689

relationships with medical staff"); d) convenience of administration (e.g. "*It allows less time spent managing asthma*"). Ratings occurred through a bipolar scale of evaluation (−2, strong belief that attributes specifically characterize SC; −1 mild belief that attributes specifically characterize SC; 0 = attributes characterize both modalities equally; 1 = mild belief that attributes specifically characterize IV; 2 = strong belief that attributes specifically characterize IV). The content of the 13 selected items based on factor analysis is reported in Table 1.

Additionally, patients were asked to choose either IV or SC route of administration in case their attending physician would have prescribed them a biologic therapy (Additional file 3).

Statistical analysis

Means and standard deviations or absolute and relative frequencies were respectively computed for continuous or categorical variables.

The association between patients' preference for IV or SC route of administration and socio-demographic and clinical characteristics has been evaluated with *t*-test or χ^2 test for continuous or categorical variables respectively. We adopted a stepwise logistic regression (entry criterion: $p < 0.030$; stay criterion: $p < 0.010$) to assess independent correlates of IV or SC route of administration. We adjusted the multivariable model for socio-demographic (age, sex, geographic area, employment status, high-risk occupation) and clinical characteristics (disease duration, ACQ-6 score, complexity of treatment regimen, exacerbation remedies, current and previous medication for asthma, medical resources utilization, mental and physical SF-12 composite scores, sleep quality, BMI, work productivity and activity impairment, suffering from allergy, experience with biologic therapy for asthma). $P < 0.05$ was considered statistically significant.

In order to help facilitate the interpretation of the multivariable analysis and the impact of the cross-interaction observed, we calculated the predicted probability of preferring the IV administration route for ten hypothetical patients with different demographic characteristics, clinical factors and beliefs, based on the estimated parameters of the logistic regression (Table 2). Factor analysis and related reliability concerning beliefs towards IV and SC route of administration are shown in Table 1. Analyses were conducted with SAS 9.4 ™.

Results

One hundred and fifty patients fulfilled the inclusion criteria and completed the questionnaire. Table 3 shows socio-demographic and clinical characteristics of the whole sample and the subset of patients who expressed preference for IV (18.7%) or SC (81.3%) route of administration.

In total, half of the sample (50.7%) was currently taking corticosteroid; SC biologic therapy was the current therapy for 32% of patients (among these, 31 subjects (64.8%) were treated with omalizumab, 17 subjects (35.4%) with mepolizumab), whereas 4% had past experience with biologic drugs. Disease duration was 25 years on average (sd = 12.4), which represented about half their lives (48.8 y; sd = 12.1). In the previous 12 months, subjects had access almost twice to the emergency room (ER) and received 4.55 outpatient visits due to asthma-related complications; remedies to last exacerbation mainly consisted in corticosteroid dose escalation (1.76 times).

Table 2
Hypothetical clinical scenarios illustrating adjusted probability of preferring the IV route of administration.

Case	ACQ-6[a]	ER access[a]	Belief: speed of action[a]z	Adjusted estimated prevalence of preference for IV route of administration
A	0	1	−1	1%
B	−1	−1	−1	3%
C	−1	1	1	3%
D	1	−1	−1	5%
E	0	1	1	15%
F	1	−1	0	18%
G (reference)	0	0	0	19%
H	1	1	0	21%
I	1	1	1	52%
J	2	2	2	98%

[a] Numbers represent increase (1,2) or reduction (−1) of standard deviations from the mean of total sample (ACQ-6 score = 2.62, sd = 0.52; frequency of resorting to ER services in case of exacerbations = 0.96, sd = 0.80; speed of action of drug (belief) = 0.64, sd = 1.46). **Asthma-related treatment regimen held constant at their sample average (Regimen Complexity: 2.12; BMI: 24).

Table 3
Socio-demographic e clinical characteristics of the sample.

	Total sample N = 150	Preference for IV N = 28 (18.7%)	Preference for SC N = 122 (81.3%)	p
Age	48.8 (12.1)	52.7 (9.19)	47.9 (12.5)	0.038
ACQ-6	2.62 (0.52)	2.73 (0.71)	2.60 (0.47)	> 0.10
Complexity of treatment regimen	2.12 (0.71)	2.07 (0.77)	2.13 (0.70)	> 0.10
Last exacerbation remedies				
Corticosteroid dose escalation	1.76 (1.29)	1.25 (1.40)	1.88 (1.24)	0.028
Corticosteroid prescription	1.07 (1.02)	0.75 (0.97)	1.14 (1.02)	0.063
Hospitalization	0.55 (0.70)	0.39 (0.63)	0.58 (0.71)	> 0.10
Emergency room access	0.96 (0.80)	0.61 (0.68)	1.04 (0.81)	0.009
Body Mass Index	24.1 (2.77)	24.8 (2.66)	23.9 (2.78)	> 0.10
Time since asthma diagnosis	25.8 (12.4)	24.9 (12.7)	26.0 (12.4)	> 0.10
Medical resource utilization (previous 12 months)				
Hospitalization days	1.45 (1.72)	1.25 (1.86)	1.50 (1.69)	> 0.10
Outpatients use	4.55 (1.65)	4.46 (1.62)	4.56 (1.67)	> 0.10
Emergency room access	1.86 (1.62)	1.86 (1.94)	1.86 (1.54)	> 0.10
Mental composite score (SF 12)	54.2 (6.54)	55.1 (7.75)	53.9 (6.23)	> 0.10
Physical composite score (SF 12)	37.6 (5.59)	37.7 (6.15)	37.6 (5.48)	> 0.10
Sleep quality (0 = very poor - 10 = excellent)	5.61 (1.18)	5.46 (1.48)	5.64 (1.11)	> 0.10
Work productivity and activity impairment (WPAI)				
Sick leave (asthma related) (%)	4 (0.09)	6 (0.10)	5 (0.09)	> 0.10
Presenteeism (%)	28 (0.20)	25 (0.22)	28 (0.20)	> 0.10
Total Productivity Loss (%)	33 (0.24)	31 (0.27)	33 (0.24)	> 0.10
	N (%)	N (%)	N (%)	
Women	79 (52.7)	14 (50.0)	65 (53.3)	> 0.10
Geographic area				
North	32 (21.3)	4 (14.3)	28 (22.9)	> 0.10
Centre	47 (31.3)	12 (42.9)	35 (28.7)	
South	30 (20.0)	3 (10.7)	27 (22.1)	
Islands	41 (27.3)	9 (32.1)	32 (26.2)	
Route of administration of current asthma-related medication				
Spray	136 (90.7)	28 (100)	108 (88.5)	0.06
Subcutaneous	49 (32.7)	0	49 (40.2)	< .000
Oral	97 (64.7)	18 (64.3)	79 (64.7)	> 0.10
Current asthma-related medication				
Corticosteroid	76 (50.7)	7 (25.0)	69 (56.6)	0.003
Biologic[a]	48 (32.0)	0	48 (39.3)	
Allergy	132 (88.0)	23 (82.1)	109 (89.3)	
Previous/current experience of SC formulation of biologic therapy for asthma	54 (36.0)	5 (17.9)	49 (40.2)	0.03
Employed	116 (77.3)	20 (71.4)	96 (78.7)	> 0.10
Exposure to occupational risk (metal fumes/flour/stinging powder or gas)	82 (54.7)	19 (67.9)	63 (51.6)	> 0.10

Values are shown as mean (standard deviation, sd). P values represent confidence levels of t-test for continuous variables, χ^2 for categorical variables.
[a] SC formulation (i.e. SC mepolizumab or omalizumab) was the only anti IL-5 available route of administration at the time of the investigation.

Patients who expressed preference for IV were older (52.7 y vs. 47.9 y; p = 0.04); were less likely to escalate corticosteroid dose (1.25 vs. 1.88, p = 0.03) and to resort to ER access (0.61 vs. 1.04; p = 0.009) during asthma exacerbation; were less likely to use corticosteroid for current management of asthma (4.7% vs. 46%; p = 0.003) and to use inhalatory formulation for current medication (18.7% vs. 72%; p = 0.06).

Patients who reported previous or current experience with SC biologic therapy for asthma expressed greater preference for SC route of administration compared to IV formulation (32.7% vs. 3.33%; p = 0.03).

Associations between preferences and beliefs towards IV and SC route of administration are shown in Fig. 1. Overall, patients felt that SC was more convenient than IV; however, such belief was not associated with higher likelihood of preferring SC as a route of biologic therapy administration (−2.08 vs. −1.5; p > 0.10).

Furthermore, patients who preferred IV formulations were more likely to believe that such an administration route would enable quicker and more effective drug action (p = 0.0001), as well as procedural safety and medical oversight (p = 0.0002) and social support (p = 0.007) compared to subjects who expressed preference for SC medication.

Statistically significant predictors of preference for IV route administration in the multivariable logistic regression model are shown in Table 4. The interaction between ACQ-6 score and ER use during exacerbation was statistically significant (0.76; p = 0.04). Parameter estimates indicated that the strength of association between asthma control status and the likelihood of preferring IV formulations increased with greater use of asthma-related ER services; additionally, beliefs toward formulation effectiveness/efficiency in reducing symptoms was the only belief score independently associated with patients' preferences (Table 4). The model achieved excellent discrimination of administration route preference (area under the curve – AUC = 0.87).

In order to simplify the interpretation of regression coefficients we report ten different hypothetical clinical scenarios illustrating estimated probabilities of preferring IV route of administration associated to different values of ACQ-6 score, frequency of resorting to ER services in case of exacerbations, and beliefs toward differential efficacy across administration routes. Body mass index and the number of asthma-related treatments were held constant at the sample average (Table 2). The reference patient in our sample (case G) had 19% probability of preferring IV administration. The probability of preferring IV administration rose as the patients had more intractable disease (i.e. higher ACQ-6 score), was more likely to access ER in case of exacerbation and more strongly believed IV was more effective than SC administration.

Discussion

This study investigated preference and beliefs towards IV and SC routes of administration of biologic therapy among patients suffering from inadequately controlled severe asthma.

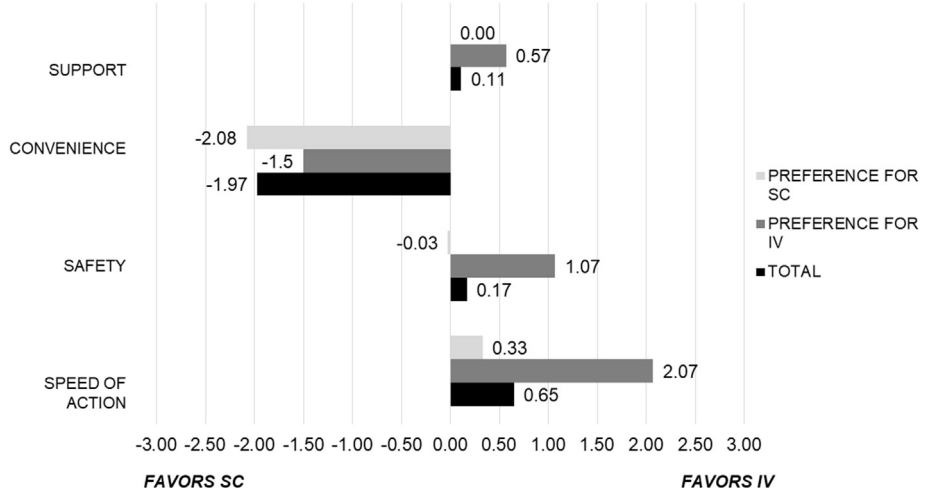

Fig. 1. Association between preferences and beliefs towards IV and SC routes of administration for total, SC and IV sample. SC = subcutaneous; IV = intravenous.

Our findings revealed SC formulation was the preferred route of administration, chosen as a hypothetical add-on therapy by more than 80% of participants.

Patients' beliefs toward procedural safety and medical oversight, social support, efficacy and speed of action were associated with administration route preference in the univariate analysis. However, multivariable logistic regression showed that only beliefs toward efficacy independently affected likelihood estimates. Given the relatively small sample size and the inter-correlation between beliefs dimensions, it may not be possible to disentangle the independent effect of each belief within this study. Even though multicollinearity was moderate in our analysis, we cannot exclude that regression estimates were unstable (i.e. sensitive to small changes) and overly imprecise (i.e. wider confidence intervals due to multicollinearity).

We also showed that patients with less asthma control were more likely to opt for IV formulation, especially when accesses to ER services in case of exacerbations were frequent. Taken together, our results suggest that patients may perceive IV treatment as a more effective drug, reserved for the most severe or difficult-to-control cases.

Since we observed that patients' beliefs towards route of administration may influence their treatment preferences, it is important to explore in more detail specific beliefs driving patients' scale scores. Specifically, our results showed that SC formulation was felt as enabling more time for daily activities unrelated to disease care (loading = 0.78), as well as allowing greater convenience compared to IV formulation (loading = 0.73) and was believed to impose less time spent managing asthma (loading = 0.75) and its practical hassles concerned to treatment administration (loading = 0.70). Conversely, IV route of administration was associated with less frequent dose administrations (loading = 0.83), considered faster in reducing symptoms (loading = 0.74) and more effective (loading = 0.52) compared to SC formulation. Such beliefs were stronger for patients who expressed preference for IV administration, and it was the most important predictor of IV preference.

Table 4
Statistically significant predictors of preference for IV route of administration.

	Estimates	p
ACQ-6	1.04	0.011
ACQ-6 * ER access (exacerbation remedy)	0.76	0.040
ER access (exacerbation remedy)	−0.68	0.064
Belief: speed of action	1.44	< 0.0001
Number of asthma-related treatment	0.78	0.068
BMI	0.18	0.067

Multivariable model adjusted for socio-demographic (age, sex, geographic area, employment status, high-risk occupation) and clinical characteristics (disease duration, ACQ-6 score, complexity of treatment regimen, exacerbation remedies, current and previous medication for asthma, medical resources utilization, mental and physical SF-12 composite scores, sleep quality, BMI, work productivity and activity impairment, suffering from allergy, experience with biologic therapy for asthma).

Since only a minority (36%) of our sample reported current or previous treatment with SC biological drugs for asthma, and none had experience with IV biologics, understanding whether observed beliefs may rely on false opinions is crucial to informed decision-making.

Indeed, previous studies investigating preference for IV or SC formulation mostly evaluated patients' perspective after they switched from one route of administration to another, thus considering directly experienced trade-offs: compared to IV formulation, SC was frequently associated with convenience of use since the self-administered procedure resulted in considerable time savings for patients.[11,18] Conversely, both IV and SC biologic therapy for uncontrolled asthma require a hospital care setting for administration, which may thus virtually eliminate the differences across the two formulations in terms of administration time and organizational burden for the patient; our questionnaire specifically tapped administration time intrusiveness on daily life and organizational burden. Unfortunately, we could not debrief patients' cognitive answering process to discover how their beliefs were formed. Such understanding is key to delivering appropriate health education and correct unfounded beliefs which may affect treatment expectations, decisions and subsequent treatment satisfaction.

Similar to opinions about convenience, beliefs toward efficacy and speed of action should be challenged against scientific evidence. Few studies compared asthma-related drugs with different administration routes generally showing no statistically significant difference.[22] One notable exception is represented by one randomized controlled trial (RCT) comparing 4 monthly doses of IV reslizumab against SC mepolizumab (12 monthly doses). The authors observed greater asthma control among patients on IV reslizumab compared to the comparators in a subset of severe prednisone-dependent patients with asthma.[24] However, it is not currently possible to discriminate the effect of the active principle and the impact of the administration route.

Other potentially important beliefs dimensions have been investigated. Previous studies assessing experience with IV biologic therapies among Inflammatory Bowel Disease and rheumatology patients, showed satisfaction with IV treatment because it was associated with enhanced social support and closer procedural oversight from health care professionals and physicians.[13] In our study, neither social support nor procedural oversight was felt as a prominent feature of any specific

administration and this may be consequently due to lack of experience with biologic therapy; however, patients preferring IV formulations were more keen to believe that this route of administration would guarantee a greater procedural safety and medical oversight.

Given that asthma-related biologics are all administered in hospital settings, and RCTs have proven both mepolizumab, reslizumab and benralizumab to be safe,[13] reasons driving patients' beliefs should be investigated further.

Finally, this study has some limitations. First, it is a cross-sectional survey, and our patients have been invited to speculate on a hypothetical scenario since, at the time of the survey, no IV formulation was marketed worldwide. As a consequence, we cannot directly infer actual behavior should the patients face a real option. Moreover, we acknowledge that the inclusion of patients with a previous or current experience of biologic treatment may represent a confounder; in this view, the multivariate model was adjusted for treatment regimens and previous biologics use. Indeed, we believe that the study sample could reflect a real life clinical scenario in outpatient clinics that are responsible for the everyday management of patients with asthma. Second, the beliefs toward administration modality scale (BAM) was developed for the study since no existing questionnaire tapped the dimensions of interest. Even though the basic psychometric properties corroborated the suitability of BAM among patients with uncontrolled asthma, further studies should replicate our results. Finally, recruitment was based on a patients' self-administered screener questionnaire. As a result, we cannot exclude selection bias limiting the generalizability of the study.

Conclusions

This study investigated preferences and beliefs towards IV and SC route of administration among patients with severe uncontrolled asthma reporting limited experience with biologic therapies. We found preference to be guided by partially misleading beliefs, which may generate wrong expectations that in turn may affect treatment satisfaction and adherence; clinicians should be aware of possible cognitive bias in order to provide patients with correct information and health education. Overall, our findings suggest that beliefs toward convenience and efficacy of drugs with different routes of administrations should be formally elicited and discussed during doctor-patient interaction to achieve informed shared-decision making.

Patients with severe asthma are at risk of increased morbidity and have a substantial impact in terms of healthcare utilizations; thus identifying optimal treatment regimen is fundamental.[20] In light of similar efficacy and safety profiles of identified medications, patients' preference assumes a relevant role thus making a shared decision with clinicians on realistic information essential. Further studies are needed to deeply investigate preference among patients with uncontrolled severe asthma, and to determine their role over compliance, satisfaction and perception of treatment efficacy.

Declarations

Ethics approval and consent to participate

Not applicable. According to the Italian regulation cross sectional survey researches based on anonymous questionnaire does not require ethical committee approval.

Consent for publication

Not applicable.

Availability of data and material

The datasets analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

PS reports grants and personal fees from Chiesi Farmaceutici, grants from AirLiquide, Pfizer, Almirall, personal fees from Astra Zeneca, Boehringer Ingelheim, Novartis, Menarini, Malesci/Guidotti, Mundipharma, Zambon, **Berlin-Chemie, Valeas**. DR reports personal fees from Astra Zeneca and Boehringer Ingelheim. FB has participated as a lecturer, speaker, and/or advisor in scientific meetings and courses under the sponsorship of Astra Zeneca, Biofutura, Boehringer Ingelheim, Chiesi Farmaceutici, Dompè, GlaxoSmithKline, Lallemand Pharma, Malesci/Guidotti, Menarini, Mundipharma, Novartis, Teva, and Zambon.

MF, IB and AF declare that they have no competing interests.

Authors' contributions

PS, IB, AF and FB participated in study design and data analysis; PS, MF, IB, DR, F and FB participated to data interpretation and manuscript and drafting. All Authors critically revised the manuscript and gave final approval.

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Authors' information

Not applicable.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.waojou.2019.100030.

List of abbreviations

ACQ-6	Asthma Control Questionnaire 6-item score
BAM	beliefs toward administration modality scale
BSQ	brief screener questionnaire
CS	subcutaneous
ER	emergency room
IL	interleukin
IV	intravenous
SDM	shared decision making
mAbs	monoclonal antibodies

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